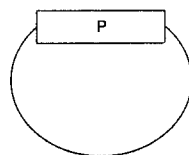**1.** **CLAIM AMENDMENTS (LISTING OF CLAIMS):**

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 32-35, 39, 40, 51 and 52 have been indicated as allowed in the instant Action.
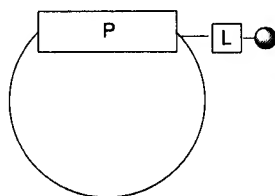
1-7.   (Canceled)

8.   (Currently Amended)   A method of synthesis of a cyclic peptide or peptidomimetic compound of General Formula I

General Formula I
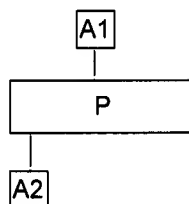
or General Formula II

General Formula II

where L in General Formula II is a linker unit linking the cyclic peptide to a solid support

 , in which the cycle is a monocycle, bicycle or higher order cyclic peptide or

peptidomimetic compound comprising 2 to 15 monomers, which is carried out in solution, comprising the steps of:

a)   Preparing a linear peptide or peptidomimetic compound of General Formula III

```
        ┌──┐
        │A1│
        └──┘
         │
   ┌─────────────┐
   │      P      │
   └─────────────┘
    │
  ┌──┐
  │A2│
  └──┘
```
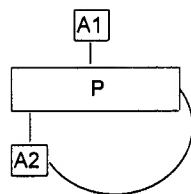
General Formula III

where P is a linear peptide or peptidomimetic compound of 2 to 15 monomers;

A1 is one or more N-substituents, either reversible or non-reversible, on the peptide backbone, or is a chemical moiety that forces a *cis* conformation of the backbone, and

A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide;

b)   Activating the *C*-terminus to form a cyclic peptide or peptidomimetic compound of General Formula IV:

3

General Formula IV

c)   Permitting the peptide or peptidomimetic compound of General Formula IV to rearrange *via* a ring contraction reaction to form a cyclic peptide or peptidomimetic compound of General Formula V; and ~~optionally~~
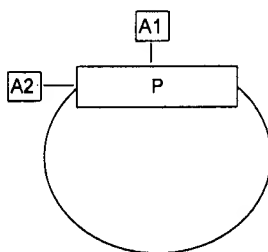
General Formula V

d)   Subjecting the cyclic peptide or peptidomimetic compound of General Formula V to a deprotection reaction to remove the <u>A1 and A2</u> groups ~~A1 and A2~~ to yield the desired cyclic peptide or peptidomimetic compound of General Formula I or General Formula II.

9. (Previously Presented) The method of claim 8, in which P is a linear peptide of 2 to 10 monomers.

10. (Previously Presented) The method of claim 9, in which P is a linear peptide of 2 to 5 monomers.

11. (Currently Amended) The method of claim 8, in which step d) is omitted; and either the A1 group is left attached to the peptide, or the A2 group, is left attached to the peptide or both A1 and A2 are left attached to thesaid peptide for linking it to a solid support or to another peptide or peptidomimetic compound, from which the compound of General Formula I, or the compound of General Formula II may subsequently be obtained.

12. (Currently Amended) The method of claim 11, in which: (a) A1 is subsequently linked to asaid solid support or linked to said another cyclic peptide or peptidomimetic compound; (b) A2 is subsequently linked to asaid solid support or linked to said another cyclic peptide or peptidomimetic compound; or (c) both A1 and A2 are subsequently linked to asaid solid support or linked to said another cyclic peptide or peptidomimetic compound.

13. (Previously Presented) The method of claim 8, in which A1 is a reversible N-substituent.

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14. (Previously Presented) The method of claim 13, in which A1 is a 2-hydroxy-4-methoxybenzyl, 2-hydroxybenzyl or 2-hydroxy-6-nitrobenzyl substituent.

15. (Previously Presented) The method of claim 8, in which A2 is eliminated by spontaneous ring contraction.

16. (Previously Presented) The method of claim 8, in which A2 comprises a nucleophile that reacts rapidly with a C-terminus to form an initial large ring, which then contracts either spontaneously, or upon heating or additional chemical treatment.

17. (Previously Presented) The method of claim 16, in which A2 is thiol or hydroxyl.

18. (Currently Amended) The method of claim 8, in which A2 is an irreversible substituent, A2 is removed after ring contraction[[,]] or [[A2]] is eliminated spontaneously upon ring contraction.

19. (Previously Presented) The method of claim 8, in which A2 is formed by reacting an amino nitrogen in P with a compound of general formula:
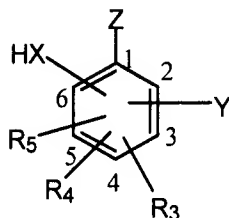
in which the ring:

(a)   is an aromatic 6-membered ring;

(b)   comprises 3 carbon atoms substituted respectively by XH, Z and Y; and

(c)   is additionally substituted,

in which

X is oxygen, sulfur, CH_2O-, or CH_2S-;

Y is an electron-withdrawing group;

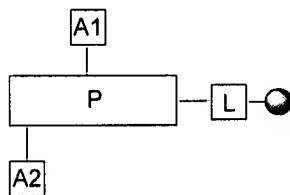Z is any group which allows the formation of a covalent carbon-nitrogen bond; and

R^3, R^4 and R^5 are each independently hydrogen, alkyl, aryl, arylalkyl, heteroaryl, alkoxy, aryloxy, XH or Y, or a covalent linkage to a solid support, and

in which R^3 and R^4 or R^4 and R^5 can optionally together with the ring form a 5-, 6-, or

7-membered ring.

20-31. (Canceled)

32.   (Previously Presented) A method of solid phase synthesis of a cyclic peptide, comprising

the steps of:

a)   synthesis of a linear solid support-bound peptide of General Formula XIII,
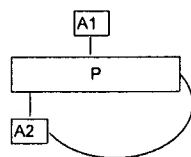

General Formula XIII

where P is a linear peptide of 2 to 15 monomers;

A1 is one or more N-substituents, either reversible or non-reversible, on the peptide

backbone, or is a chemical moiety that forces a *cis* conformation of the backbone,

and

A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an

initial large cyclic peptide prior to ring contraction to the desired substituted
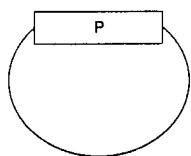
cyclic peptide;

L is a linker between any atom of the peptide and the solid support; and

b)   subjecting the peptide of General Formula XIII to cyclization and concomitant

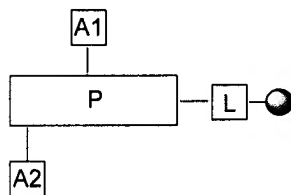cleavage from the solid support to yield a cyclic peptide of General Formula XIV,

General Formula XIV

c)   subjecting the cyclic peptide of General Formula XIV to ring contraction, and

d)   if A1 is a reversible substituent, cleaving the groups A1 and A2 to yield the

desired cyclic peptide of General Formula I:

33.   (Previously Presented) A method of solid phase synthesis of a cyclic peptide, comprising the steps of;

a)   synthesis of a linear solid support-bound peptide of General Formula XIII,

where P is-a linear peptide of 2 to 15 monomers;

A1 is one or more N-substituents, either reversible or non-reversible, on the peptide backbone, or is a chemical moiety that forces a *cis* conformation of the backbone, and

A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide;
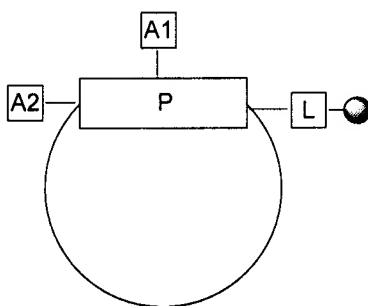
L is a linker between any atom of the peptide and the solid support, and

b)   subjecting the linear peptide to cyclization on the solid support to yield a cyclic
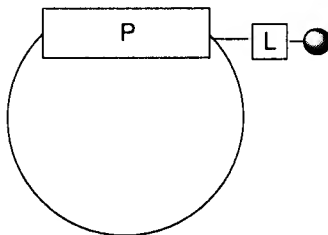
peptide of General Formula XV,
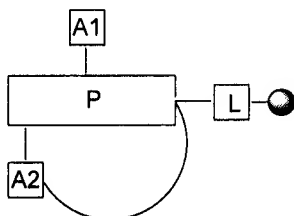
General Formula XV

c)   subjecting the cyclic peptide to ring contraction to yield a cyclic peptide of
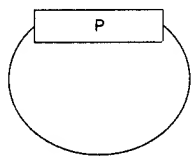
General Formula XVI,

General Formula XVI

and either

d)　　cleaving groups A1 and A2 while the peptide is bound to the solid support to

yield a resin-bound cyclic peptide of General Formula II, or

General Formula II

e)　　subjecting the cyclic peptide to deprotection and concomitant cleavage from the

solid support to yield the desired cyclic peptide of General Formula I

34.　　(Previously Presented)　The method of claim 33, in which side chain deprotection of the

peptide, removal of A1 and cleavage from the solid support are performed separately.

35.　　(Previously Presented)　The method of claim 33, in which side chain deprotection of the

peptide, removal of A1 and cleavage from the solid support are performed concurrently.

36-38. (Canceled)

39.   (Previously Presented) The method of claim 32, in which one or more of the monomers carries a side chain protecting group.
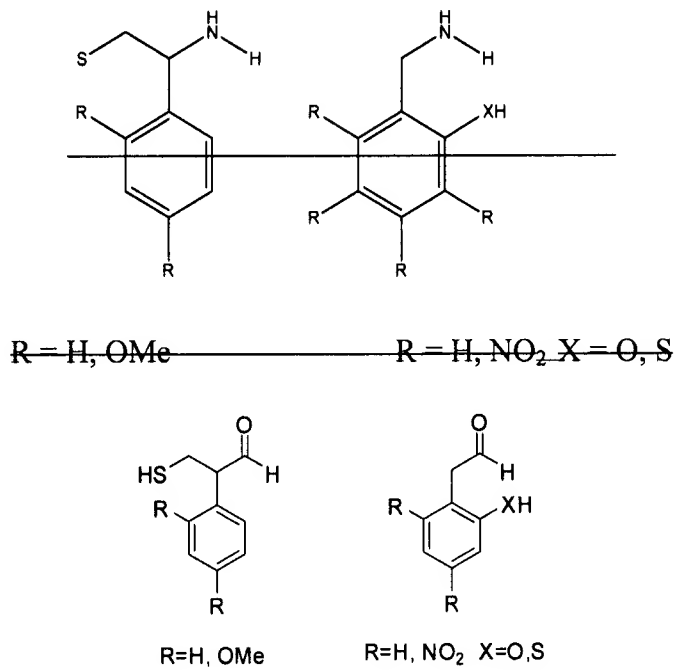
40.   (Previously Presented) The method of claim 33, in which one or more of the monomers carries a side chain protecting group.

41-43. (Canceled)

44.   (Previously Presented)   The method of claim 8, in which A1 is a *cis*-amide bond surrogate.

45.   (Previously Presented) The method of claim 44, in which the *cis*-amide bond surrogate is a tetrazole.

46. (Currently Amended) The method of claim 8, in which A2 is <u>derived from a ring</u>

<u>contraction auxiliary</u> selected from the group consisting of:

~~R = H, OMe~~ ~~R = H, NO₂ X = O, S~~

R=H, OMe   R=H, NO₂ X=O,S

<u>wherein said auxiliary facilitates contraction of said ring to form said cyclic peptide or</u>

<u>said cyclic peptidomimetic.</u>

47. (Previously Presented) The method of claim 8, in which A2 is 6-nitro-2-hydroxybenzyl,

4-nitro-2-hydroxybenzyl or 5-nitro-2-hydroxybenzyl.

48.   (Currently Amended) The method of claim 19, in which [[A2]]said compound is selected

from the group consisting of:
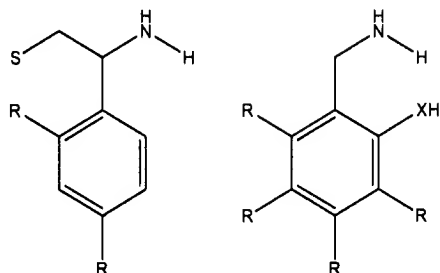
R = H, OMe   R = H, NO$_2$ X = O, S

wherein said auxiliary facilitates contraction of said ring to form said cyclic peptide or

said cyclic peptidomimetic.

49.   (Previously Presented) The method of claim 19, in which A2 is 6-nitro-2-hydroxybenzyl,

4-nitro-2-hydroxybenzyl or 5-nitro-2-hydroxybenzyl.

50.   (Previously Presented) The method of claim 8, in which the ring contraction reaction

occurs spontaneously.

51.   (Previously Presented) The method of claim 32, in which the ring contraction reaction

occurs spontaneously.

52.   (Previously Presented) The method of claim 33, in which the ring contraction reaction

occurs spontaneously.